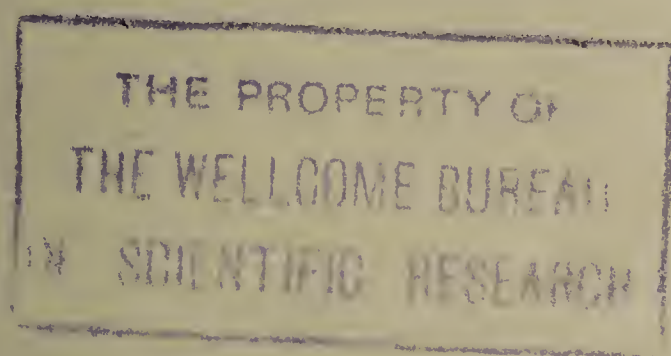


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In Memoriam

Waldemar Mordecai Wolff Haffkine

Born 15(3) March 1860. Died 26 October 1930



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THE death of W. M. Haffkine will recall an era in bacteriology associated with the development of the principles and practice of immunisation. He was an early participator in these methods and although he added little to the fundamental principles he became widely known as the apostle of prophylactic inoculation.

The year 1880 was a notable one in bacteriology for it was then that Pasteur announced his great discovery that protection can be brought about in chicken cholera by the inoculation of the living attenuated virus of the disease. He showed that this was not an isolated experience but that the same principle could be applied to anthrax (1881) swine erysipelas (1883) and rabies (1882-1886). The scientific world was filled with praise of Pasteur for his advances in knowledge.

Apart from rabies the Pasteur method had not been applied in man. This was first done (1884) by the Spanish doctor Jaime Ferrán y Clua (1849-1929) in Asiatic cholera. He inoculated many thousands of persons with the living virus of cholera.

During the fifth pandemic of cholera Egypt was invaded and commissions from Germany and France were sent to study the disease. It was in Alexandria (1883) that Robert Koch first found the comma bacillus. From Egypt, cholera was transhipped to Marseilles and from there it spread to Spain, in Alicante and parts of Lerida and Valencia.

Ferrán (1885) investigated the disease by primitive methods; he inoculated guinea-pigs with the virus and found that they became immune and he then inoculated himself and his co-worker, Dr Pauli, with living cholera material. This was in Tortosa (Ferrán's birthplace) in Tarragona. He also inoculated persons in Alcira (Valencia) and within five months he had made 150,000 inoculations on more than 50,000 persons.

Newspaper reports of these events aroused great interest and a Spanish Commission was appointed to investigate Ferrán's methods and claims. It reported that Ferrán was a man of science, probity and good faith, that his inoculations were not dangerous and that statistics seemed to be in favour of inoculation as a prophylactic. Ferrán took no part in the political squabbles which followed the report of the commission and a second commission was appointed to accompany Ferrán to the parishes that petitioned for his services.

The French Minister of Commerce sent M. Gibier to report upon Ferrán's method and accompanying him was the well-known Belgian bacteriologist, van Ermengem. Later, Professor Brouardel was sent along with Albarran and Charrin. A writer of the period expressed himself forcibly when he said that "arrogant, supercilious pseudo-patriotism on the part of the French, disdaining to learn anything from an obscure corner of a less eminent neighbouring nation, and the indignant self-respect, conscious capacity and the probity of the Spaniard made this mission an utter failure at the end of three days" when they returned to Paris. They published a report of their mission and described Ferrán's methods and his defective microscopes.

Klein in England wrote that Ferrán was comparable to Don Quixote rather than to Edward Jenner. Van Ermengem seems to have been more fortunate in his relations with Ferrán and he described how the vaccine was prepared in porringers covered only with a sheet of paper. Ferrán's microscope had no oil immersion and no condenser and he used no stains. Van Ermengem, an exceedingly accurate worker with a wide knowledge of the cholera bacteriology of that day, was permitted to examine Ferrán's vaccine and found it was a pure culture of cholera vibrio "sans melange avec un autre organisme" which must be regarded as "one up" for Ferrán, despite his prehistoric methods.

It is now admitted that it was Ferrán who (1885) first applied the Pasteur principle in man by inoculating living attenuated cultures of Asiatic cholera.

The risk of injury from living cultures led about this time to the study of other methods and it was in 1886 that D. E. Salmon and Theobald Smith showed that it is possible to produce immunity by the inoculation of cultures killed by heat. This made inoculation a much safer practice. I have mentioned these things in detail as they were thoroughly well known years before Haffkine ever wrote on the subject and the claims made for him as the discoverer of vaccines may be regarded as quite inaccurate.

WALDEMAR MORDECAI WOLFF HAFFKINE was born in Odessa, 15(3) March 1860, son of Aaron Haffkine of Odessa and Rosalie, daughter of David-Aïsic Landsberg. He received a classical training at Berdjansk, on the Sea of Azov, 300 miles east of Odessa.

From 1879-1883 he studied science in Odessa under Elie Metchnikoff (1845-1916) who at that time was professor of zoology there, and who went to Paris, 1888, where he became one of heads of laboratories in the newly erected Institut Pasteur. Haffkine worked in the zoological museum at Odessa from 1882-1888 and then turned his footsteps to the Occident halting for a short time in Geneva to earn a little money. This spent, he arrived in Paris in a state bordering on destitution and implored his old teacher Metchnikoff to procure a post for him in the Pasteur Institute. The only post available at the time was that of librarian which he accepted at a pittance. His time as librarian was not fully occupied and he was able to do some scientific work in Metchnikoff's laboratory. This bore fruit in the publication of two papers in the *Annales de l'Institut Pasteur* in 1890 vol. iv. The one was entitled "Maladies infectieuses des paramécies" the other "Recherches sur l'adaptation au milieu chez les infusoires et les bactéries." Neither was of great importance.

Two years later appeared a short paper of two pages entitled "Le Choléra asiatique chez le Cobaye" (*Compt. rend. Soc. de Biol.*, 1892, 9 s., iv. 635-637). This is one of Haffkine's principal, published efforts and described methods of attenuation and exaltation of the cholera vibrio. For attenuation he utilised the method of Roux and Yersin by cultivation in a current of air, and he claimed that he had exalted the virulence of the vibrio to a condition of "virus fixe" by passage through the guinea-pig peritoneum. He also stated that an inoculation of attenuated culture determined immunity against the "virus fixe." The paper contains general statements rather than experimental details. It was followed by another trivial communication occupying $8\frac{1}{2}$ lines on cholera in the rabbit and pigeon and confirming what he had already stated concerning cholera in the guinea-pig. In the same year (1892) appeared another short communication (*Compt. rend. Soc. de Biol.*, 1892, 9 s. 740) entitled "Inoculations de vaccins anti-cholériques à l'homme." In this he described the effects of cholera inoculation (18th July, iv, 1892) on himself and on his friends Dr Iawein of St Petersburg, Dr Tamancheff of Tiflis and M. Wilbouchewitch an engineer from Moscow. Haffkine concluded from this small series that two inoculations of cholera vibrios are harmless and he added "J'exprime l'espoir que six jours après la vaccination l'organisme de l'homme aura acquis l'immunité contre l'infection cholérique."

With great boldness and in the belief that he had made an important discovery Haffkine now conceived a plan of inoculating human beings on a grand scale in the hope that cholera could be prevented and epidemics of this dreaded disease would cease. India appeared the proper *locus* for this attempt and to India Haffkine decided to go. Through the influence of the Marquis of Dufferin and Ava, at that time British Ambassador in Paris (1891-1896) following

his successful term (1884-1888) as Governor-General of India, he was brought into touch with the proper authorities and he came to England, preparatory to launching his Indian campaign. Here he gave some demonstrations and finally proceeded to India, 1893.

During his first year (April 1893 to March 1894) cholera inoculations were performed in the North-West Provinces and Oudh and in the Punjab. The total number of persons treated was 22,703, partly Europeans, civil and military, Hindoos, Mohammedans, Sikhs—princes, noblemen and labourers. Haffkine's activities spread as far as Rawal Pindi and Peshawar. This was a district of nervous political tension and there were not wanting those who hinted that Haffkine—a Russian—had intentions other than those of a peaceful inoculator. Inquiries showed however that he was politically perfectly harmless and that his aims were purely scientific and humanitarian. His activities in the second year (1894-1895) were however transferred to Lower Bengal and Assam and in those regions he inoculated 19,473 persons with his cholera vaccine. It is not apparent from Haffkine's writings whether the cholera vaccine was a living culture or dead, and doubts were expressed as to its real value. W. F. Harvey (*M.R.C. System of Bacteriology*, vol. iv., p. 420) says the results were "surprisingly slight" and he quotes the figures of Haffkine of morbidity and mortality these being 13·53 per cent. and 66 per cent. respectively among the inoculated as against 18·75 per cent. and 72 per cent. among the uninoculated.

While the cholera inoculations were progressing in India, bubonic plague had developed in Bombay and the Government of India entrusted Haffkine with the preparation of a plague vaccine. His first publication "Remarks on the plague prophylactic fluid" appeared in the *British Medical Journal*, 1897, i. 1461. The prophylactic was a killed culture of *Bacillus pestis*. Haffkine to his credit first tried the prophylactic on himself (10th January 1897) and then applied it to volunteers in Bombay to the number of several hundreds. In the course of a few weeks 8142 persons were inoculated. As the epidemic progressed more and more were inoculated until finally an enormous technical organisation was employed to produce millions of doses of the plague prophylactic. A laboratory was started by Haffkine at Byculla in 1896 and in 1893 was moved to Parel and was called the Plague Research Laboratory. At a later period it was called the Bombay Bacteriological Laboratory and in 1925 it was renamed the "Haffkine Institute." The English Indian Plague Commission in its Report (vol. v. p. 268) expressed its sense of the importance of the method which Mr Haffkine devised and of the results which were achieved by it. "The credit due to Mr Haffkine" says the Commission "is the greater because the difficulties with which he has had to contend in this matter could only have been overcome by great zeal and endurance. Mr Haffkine's work while not based on any new

scientific principle constitutes, it seems to us, a great practical achievement in the region of preventive medicine."

Despite all that Haffkine could do the plague increased apace and the manufacture of plague vaccine grew proportionately. In 1902-3 more than half a million persons were inoculated. The strain on the technical methods began to show itself. On 30th October 1902, 107 persons were inoculated at Mulkowal and of these 19 were affected with and died from lockjaw. They had all been inoculated from the same bottle. A great deal was written about the "Mulkowal disaster" which was investigated by a commission in India and subsequently submitted for examination by the Lister Institute. On 1st December 1906 the Government of India issued in Calcutta in the form of a supplement to the *Gazette of India* a pile of documents relative to the case.

Haffkine's control was suspended for a time and he remained unemployed until he received new terms of appointment in India. He was made Director-in-chief and officer-in-charge of the Biological Laboratory in Calcutta. He retired in 1915, left India and settled in Paris at Boulogne-sur-Seine.

Before he left India he had become somewhat overbearing and showed some eccentricities which became more accentuated as time went on. He refused to allow any animal experiments to be carried out in his laboratory, and he adopted some of the tenets of the Jains, a religious community in India who believe in non-injury (ahimsā) of any living thing. Haffkine once flew into a passion because one of his assistants was found dissecting the still warm proglottis of a tape-worm. He spent much time in studying the Bible and often remarked that he was an apostle sent by God for the relief of suffering of mankind and in particular the Jews.

Haffkine did not consider himself to be a mere bacteriologist. He ranged himself alongside the trinity of Jenner, Pasteur and Lister and in his later years was disappointed that the world had not taken him wholly at his own estimate. Haffkine was a clean-shaven rather handsome man in his earlier years. He was made C.I.E., 1897. He wrote 35 papers but few of these were strictly speaking the record of scientific research given in detail. Many were lectures and were usually published in several journals and weeklies at the same time, or in special reports not easy to identify or locate in libraries.

W. BULLOCH.

